

REMARKS

I. STATUS OF CLAIMS

Claims 1-30 are pending, with claims 12-16, and 26-30 withdrawn from consideration, as being directed to non-elected subject matter. Claim 1 is amended to incorporate the subject matter recited in claim 2, and claim 2 cancelled accordingly. Thus, no new matter has been added by the amendments presented herein.

II. REJECTION UNDER 37 C.F.R. § 103(a)

Claims 1-11 and 17-25 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,536,469 to Jonsson et al. ("*Jonsson*") in view of Breborowicz et al. "Replacement of Glucose with N-Acetylglucosamine in Peritoneal dialysis Fluid-Experimental Study in Rats, *Peritoneal Dialysis International*, 21(Supplement 3): S365-S367 (2001) ("*Breborowicz*"). Office Action at pages 4-6.

According to the Examiner, *Jonsson* discloses a sterile medical solution containing glucose for peritoneal dialysis. See *id.* at page 4. The Examiner concedes that *Jonsson* fails to teach "a medical solution containing one or more acetylated or deacetylated amino sugars nor does *Jonsson* et al. specifically disclose the preparation of a final medical solution wherein the pH is 7.4." *Id.* at page 5. The Examiner brings in *Breborowicz* to remedy this deficiency, contending that "*Breborowicz* et al. teaches partial replacement of glucose with N-acetylglucosamine (NAG) in peritoneal dialysis fluid results in advantageous preservation of the peritoneal membrane" *Id.* The Examiner concludes that "[o]ne of ordinary skill in the art would be motivated to combine *Jonsson* et al. in view of *Breborowicz* et al. because *Breborowicz* teaches it is

advantageous to partially replace glucose with N-acetylglucosamine (NAG) . . . [and o]ne of ordinary skill in the art would be motivated to optimize the final medical solution wherein pH is 7.4 because *Jonsson et al.* teaches the final peritoneal dialysis solution optimized at a pH between 6.5 and 7.5” *Id.* at page 6. Applicants respectfully disagree and traverse the rejection in view of the following reasons.

The Examiner must make several basic factual inquiries to determine whether the claims of a patent application are obvious under 35 U.S.C. § 103. These factual inquiries, set forth in *Graham v. John Deere*, require the Examiner to:

- (1) Determine the scope and content of the prior art;
- (2) Ascertain the differences between the prior art and the claims in issue;
- (3) Resolve the level of ordinary skill in the pertinent art; and
- (4) Evaluate evidence of secondary considerations.

See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966). The obviousness or non-obviousness of the claimed invention is then evaluated in view of the results of these inquiries. *Id.*; *see also KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1734 (2007).

Based on the Supreme Court's decision in *KSR*, the Patent Office has announced seven exemplary rationales that may support a conclusion of obviousness. (*See M.P.E.P.* § 2143.) All of these bases for obviousness require that one of ordinary skill in the art, without knowing anything of the claimed invention, would not only have a reason or rationale to combine the references to produce that invention, but also would have a reasonable expectation of success and achieve predictable results. Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of

obviousness here, because one skilled in the art would not have expected, based on the cited references, that terminal sterilization could be applied to a solution comprising one or more acetylated or deacetylated amino sugars with any reasonable expectation of success.

As discussed above, *Jonsson* is silent regarding terminal sterilization of amino sugar solutions. *Jonsson* teaches only heat sterilized glucose and glucose-like compound peritoneal dialysis solutions (e.g., glucose polymers). *Jonsson* at Abstract. As a result, one of ordinary skill in the art would have had no reasonable expectation that substituting glucose and glucose-like compounds with amino sugars, would overcome the problem of the prior art (i.e., toxic glucose degradation products present in peritoneal dialysis solutions).

Breborowicz fails to provide any guidance in this regard. Although *Breborowicz* states that "partial replacement of glucose with *N*-acetylglucosamine (NAG) results in better preservation of the peritoneal membrane," *Breborowicz* applies a completely different sterilization technique –filtration– to sterilize the dialysis solution at a pH of 7.05. See page S365, ll. 33-36. Nowhere does *Breborowicz* discuss terminal sterilization at a pH of 2.5-3.5 as currently claimed, and there is no evidence that such a modification would have had a reasonable expectation of success. Applicants reiterate that prior art can only be modified or combined to reject claims as *prima facie* obvious if it would have been reasonable to expect success in doing so. M.P.E.P. § 2143.02; *In re Merck & Co., Inc.*, 231 U.S.P.Q. 375 (Fed. Cir. 1986).

One of ordinary skill in the art would not have had a reasonable expectation that the sterilization method for glucose in *Jonsson* would have been applicable to a solution comprising NAG

It is well known in the art that the heat-sterilization of solutions comprising organic components often leads to thermal degradation products. The problem *Jonsson* solved, for example, was the heat-sterilization of glucose. See, e.g., *Jonsson* at col. 1, ll. 37-43. However, because each organic product is different, suitable conditions for the heat-sterilization of solutions comprising organic materials need to be determined on an individual basis. For or this reason, one of ordinary skill in the art would not expect that the conditions employed for the heat-sterilization of a solution comprising a given organic compound could be extrapolated to a solution comprising a different product having different characteristics.

In this regard, a significant difference exists between glucose and amino sugars, wherein amino sugars contain an "amino group and possibly an acetyl group coupled to the glucose ring." Specification at 4, ll. 4-7. Because the amino group can participate in reactions different from those in which glucose can participate, some of them being influenced by temperature, one of ordinary skill in the art would not have expected that a protocol designed for the heat-sterilization of glucose, such as that disclosed in *Jonsson*, would have been successful when part of the glucose is replaced by an amino sugar.

One factor relevant to the determination of suitable conditions for the sterilization of a solution comprising a given organic compound is the degradation pathway for that compound. Knowledge about the degradation pathway of amino sugars, such as NAG, was not known prior to the present invention and, consequently, one of ordinary skill in

the art would not have had a reasonable basis to expect that the conditions disclosed in *Jonsson* for the heat-sterilization of glucose could be extrapolated to the heat-sterilization of amino sugars. Only in hindsight could a reference like *Jonsson* be alleged to approximate the method of the present invention.

The specification teaches that “the decomposition pattern for an amino sugar solution during heat sterilisation follows specific Maillard reactions giving several different toxic decomposition products.” Specification as-filed at page 9, II. 22-35. Maillard reactions *do not* take place when only glucose or glucose-like compounds are present in solution. *Id.*, see also Figures 4a to 4d, which compare the decomposition patterns of glucose-containing solutions with amino sugar-containing solutions. The number of decomposition products is much larger in the case of amino sugar-containing solutions due to the Maillard reactions. *Id.* However, in contrast to glucose, “none of the known glucose degradation products has been found in heat sterilized NAG solutions.” *Id.* at page 3, line 36 - page 4, line 1. Thus, Applicants submit that one of ordinary skill in the art at the time of the invention, without knowledge of the particular degradation pathway of amino sugars, and without knowledge that heat sterilized NAG solutions would not comprise glucose degradation products, would have had no reasonable expectation of success in applying terminal sterilization to an amino sugar solution.

Based in part on this knowledge, unknown in the art before this invention, Applicants were able to design a protocol for the successful heat-sterilization of solutions comprising amino sugars.

In the absence of some guidance regarding the thermal degradation of amino sugars, one of ordinary skill in the art would not have had an expectation of success when applying *any* of the known heat-sterilization protocols to solutions comprising amino sugars, including that of *Jonsson*.

Applicants also note the Examiner's inclusion of U.S. Patent No. 3,697,652 to Rovati et al. ("Rovati") at page 3 of the Office Action. The Examiner states that Rovati "teaches that it is well known to heat sterilize solutions comprising N-acetylglucosamine." *Id.* Applicants respectfully submit, however, that Rovati neither anticipates, nor renders obvious the presently pending claims, at least because Rovati fails to teach, suggest, or disclose heat sterilization of solutions comprising N-acetylglucosamine in a pH range of 2.5-3.5. Indeed, Rovati teaches in Example 5, a pH range of 8.2-8.3, and further implies that adjusting the pH will have a "detrimental effect" on the N-acetyl compounds disclosed therein.

Accordingly, Applicants submit that the rejection under 35 U.S.C. §103(a) is improper and request the withdrawal of this rejection.

III. DOUBLE PATENTING REJECTION

Claims 1-11, and 17-25 have been "provisionally rejected on the ground of nonstatutory double patenting" as allegedly being unpatentable over claims 1-4, 7-12, 18-19, and 21-24 of copending Application No. 10/538,791. Office Action at pages 7-8. Applicants respectfully disagree. However, Applicants request that the Examiner hold the rejection in abeyance until the indication of otherwise allowable subject matter.

IV. CONCLUSION

In view of the foregoing remarks, Applicants respectfully requests reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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